

### Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

Claim 1, 2, 5, and 7 have been amended, claims 3, 4, and 6 have been cancelled without prejudice, and new claims 9-19 have been added. Descriptive support for new claims 9 and 10 appears in the first full paragraph on page 30 and the third full paragraph on page 35, respectively; descriptive support for new claims 11-13 appears in the first full paragraph on page 34; and descriptive support for new claims 14 and 15 appears in the first full paragraph on page 30. New claim 16 finds descriptive support in original claim 3 (i.e., claim written in independent form), and new claims 17-19 find descriptive support in original claims 3 and 6-8, respectively. Claims 1, 2, 5, and 7-19 are pending.

The amendments to the specification are made to correct typographical errors. In particular, the paragraph on page 103 is corrected to render the specification internally consistent. The specification at page 58, lines 17-18, clearly recites that *holB* was not identified by Deckert et al., 1998. Therefore, correction of the paragraph on page 103 does not constitute new matter.

The objection to the specification is overcome by the above amendments. Although applicants disagree with the assertion made by the U.S. Patent and Trademark (“PTO”), the present claim language is clearly supported by the first full paragraph on page 30, along with the disclosure of the nucleic acid sequence of SEQ ID NO: 147 and the corresponding amino acid sequence of SEQ ID NO: 148.

The objections to claims 1, 3 and 4 are overcome by the above amendments and should be withdrawn.

The rejection of claim 5 under 35 U.S.C. §112 (second paragraph) for indefiniteness is respectfully traversed. The PTO has taken the position that the term “purified” is unclear in view of the language “isolated” as used in claim 1. Applicants respectfully disagree.

The term “isolated” connotes that the claimed complex is in an environment that is distinct from that of the native complex, i.e., the complex no longer exists in a cellular environment. In contrast to a complex that can exist, for example, in a protein extract obtained from a cell, a purified complex is one that is substantially separated from other

proteins (i.e., beside those other proteins that form the complex). Both isolated delta prime subunit and purified delta prime subunit are described in the procedure recited in Example 20 for the recombinant expression of *A. aeolicus* delta prime subunit. In particular, Example 20 describes cell lysate containing the recombinant delta prime subunit (i.e., isolated but not yet purified protein), as well as the purification of delta prime subunit from the cell lysate (first via Sepharose column and then via Agarose column). Formation of a purified *A. aeolicus* clamp loader complex is described in Example 24 (purified via MonoQ column). Thus, “purified” and “isolated” are distinct terms, and persons of skill in the art would understand the distinction between these two terms.

For these reasons, the rejection of claim 5 is improper and should be withdrawn.

The rejection of claims 1, 2, and 4-8 under 35 U.S.C. §112 (first paragraph) as lacking written descriptive support is respectfully traversed.

The burden of establishing that an application lacks adequate written descriptive support falls on the PTO. *See In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976) (“[T]he PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims.”). Hence, the PTO must demonstrate *why* the disclosure is insufficient.

The Federal Circuit has clearly espoused that *per se* conclusions of written description violations cannot be founded upon the basis of genus size alone. *See Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 1326-27, 63 USPQ2d 1609, 1614-15 (Fed. Cir. 2002) (refusing to adopt position that three species as a matter of law cannot satisfy written description requirement for significantly larger genus). Thus, the PTO’s conclusion cannot be based on genus size alone. But that is precisely what the PTO has done at page 4 of the outstanding office action. Because the PTO’s position is unsupported by law and unsupported by any facts other than genus size, applicants submit that the PTO’s position cannot be sustained.

Applicants submit that the language recited in claim 1 is precisely the type of claim language that was acknowledged in *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) as being acceptable under the written description requirement. In *Eli Lilly*, the Federal Circuit addressed the validity of several claims of U.S. Patent No. 4,652,525 to Rutter et al. (“Rutter”), specifically those claims that recited the limitations ‘vertebrate,’ ‘mammalian,’ or ‘human’ cDNA for insulin. Rutter disclosed the

nucleotide and amino acid sequences of a rat cDNA encoding insulin, and described a general procedure for obtaining the human cDNA encoding insulin. *Id.* at 1567, 43 USPQ2d at 1405. The Federal Circuit found that the description of the rat cDNA did not provide adequate descriptive support for the narrow subgenus of ‘human’ cDNA (no species disclosed), the larger subgenus of ‘mammalian’ cDNA (only the one rat species disclosed), and the larger genus of ‘vertebrate’ cDNA (only the one rat species disclosed). *Id.* at 1567-68, 43 USPQ2d at 1405. The Federal Circuit did acknowledge, however, the district court’s statement that the specification provided adequate written descriptive support for the subgenus of ‘rat’ cDNA encoding insulin. *Id.* at 1566.

Thus, functional language should be acceptable when the genus as claimed is sufficiently limited in scope (i.e., from *Thermotoga* or *Thermotoga maritima*) and the specification describes one or more species within that genus. Claim 1 recites the same type of functional claim language that was identified as acceptable in *Eli Lilly* given the description of a single species by its nucleotide sequence. Thus, it should be evident that claim 1 (and claims dependent thereon) finds written descriptive support in the present application.

In view of all of the foregoing, applicants submit that the rejection of claims 1, 2, and 4-8 is improper and should be withdrawn.

The rejection of claims 1, 2, and 4-8 under 35 U.S.C. §112 (first paragraph) for lack of enablement is respectfully traversed.

It is the position of the PTO that the specification does not provide sufficient guidance for making and using other delta prime proteins within the scope of the claims. Applicants respectfully disagree.

The PTO is respectfully reminded that all that is needed is objective enablement of what is claimed. *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). The present application provides the nucleotide sequence of *Thermotoga maritima holB* (SEQ ID NO: 147) and the encoded delta prime subunit (SEQ ID NO: 148). The present application further describes how one of ordinary skill can isolate homologs of the disclosed sequence (*see* page 41, line 9 to page 42, line 29; *see also* Example 20 regarding isolation of *A. aeolicus holB*), express the delta prime subunit encoded by such homologous *holB* sequences (*see* Example 20 regarding expression of *A. aeolicus* delta prime), and test the encoded delta subunit for clamp loader assembly competence (*see* Examples 24 and 25 regarding assembly of *A. aeolicus* clamp loader) and for clamp loader activity (*see* Examples 26 and 30 regarding activity of *A. aeolicus* clamp loader). Thus, one

of ordinary skill in the art would have been fully able to make and use proteins and clamp loader complexes within the scope of the presently claimed invention.

In view of all of the foregoing, applicants submit that the rejection of claims 1, 2, and 4-8 for lack of enablement is improper and should be withdrawn.

The rejection of claim 1, 2, 4, and 5 under 35 U.S.C. §102(b) as anticipated by Genbank Accession Q9WZM9 by Nelson et al. ("Nelson") is respectfully traversed. Because claim 1 has been amended to recite the limitations of claim 6, which was not rejected over Nelson, the rejection should be withdrawn.

Because 1 is allowable for the reasons noted above, applicants further submit that new claims 9-15 also are allowable. Because the PTO did not reject claim 3 (now presented in independent form as claim 16), claims 16-19 should be allowable as well.

In view of all of the foregoing, applicant submits that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

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